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Paula Hurley — Name

October 22, 2001 — Date

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the application of: Gregg Morin et al.	Art Unit: 1633
Serial No.: 09/042,460	Examiner: Sumesh Kashal, Ph.D.
Filing Date: March 16, 1998	
For: MOUSE TELOMERASE REVERSE TRANSCRIPTASE	

DECLARATION UNDER 37 CFR § 1.132

CHOY-PIK CHIU, Ph.D.

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

I, CHOY-PIK CHIU, do hereby declare as follows:

1. I am the Senior Director of Cell Biology and Pharmacology at Geron Corporation, an owner of the invention claimed in this patent application. A copy of my *curriculum vitae* accompanies this Declaration.

2. As Senior Director of Cell Biology and Pharmacology, I oversee a variety of projects relating to the commercial development of telomerase reverse transcriptase. The mouse homolog (mTERT) and its variants provide an important model for the use of telomerase reverse transcriptase in clinical medicine.

I understand the Examiner has asked whether polynucleotides encoding mTERT can be used in vivo.

3. We have used mTERT as part of a project to study the immune response to telomerase in mice. A plasmid DNA vector has been constructed in which the mTERT coding sequence is placed under control of a modified CMV immediate early promoter in the gWiz™ high expression vector from Gene Therapy Systems. The vector has been injected into the flanks of mice, and muscle tissue has been recovered after one week for analysis of mTERT expression by RT-PCR amplification. As shown in the accompanying gel, mTERT mRNA is detected in vector-treated animals, but not in animals injected with saline control.

4. We have also used mTERT as part of a project to generate a strain of telomerase knockout mice. Embryonic stem cells were treated with a vector targeted to the 5' end of the mTERT encoding sequence, thus eliminating the start codon and preventing transcription of mTERT. Correctly targeted cells were then injected into intact blastocysts, and implanted into pseudopregnant females, according to standard techniques in the generation of knockout animals. Chimeras have been obtained as indicated by coat color of the offspring, and heterozygous mTERT knockout animals are being identified by Southern analysis. These heterozygous mice will then be crossbred to obtain homozygous mTERT knockouts.

5. Work at other laboratories confirms that the mTERT coding sequence can be used in vivo. Liu et al. (Curr. Biol. 10:1459, 2000) and Yuan et al. (Genes Cells 4:563, 1999) have produced mTERT knockout mice, and studied the characteristics of tissues and cells in these mice. Gonzalez-Suarez et al. (EMBO J. 20:2619, 2001) have produced mice in which an

extra copy of the mTERT coding region is placed under the control of the keratin 5 promoter, causing elevated expression of telomerase in epithelial cells. These mice showed an increased rate of wound healing compared with wild-type littermates. (Copies of the references accompany this Declaration.)

5. I hereby declare that all statements made in this Declaration of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified statement is directed.

10/11/01
Date

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Professional Experience

1994-present	Senior Director, Cell Biology & Pharmacology Director, Cell Biology & Pharmacology Section Leader, Cell Biology & Pharmacology Staff scientist, Cell Biology Geron Corporation, California
1990-94	Staff scientist, Systemix, Inc., California
1987-90	Postdoctoral fellow, DNAX Research Institute, California. (Dr. Frank Lee).
1987	Research Fellow, Howard Hughes Medical Institute and Harvard Medical School, Massachusetts. (Dr. Bernardo Nadal-Ginard)
1985-86	Postoctoral fellow, Dana-Farber Cancer Institute and Harvard Medical School, Massachusetts. (Dr. Geoffrey Cooper)

Education

1985	Ph.D., Pharmacology, Stanford University, California
1979	B.A., Biochemistry, Vassar College, New York

Scholarships, Honors, Membership

1999-present	American Association for Cancer Research American Society of Gene Therapy
1996,98,2000	National Scientific Advisory Council, American Federation for Aging Research
1985-1987	Postdoctoral fellowship, Cancer Research Institute
1984	Frances Lou Kallman Award, Stanford University
1984	Sigma Xi
1984	Student Travel Award, American Society of Cell Biology
1983	Student Travel Award, American Society of Cell Biology
1979-present	Phi Beta Kappa
1976-1979	Vassar College Tuition Scholarship

Patents

1. International Patent Publication WO 99/20741 (published April 29, 1999). Methods and Materials for the Growth of Primate-Derived Primordial Stem Cells. Geron Corporation, A.G. Bodnar, **C.-P. Chiu**, J.D. Gold, M. Inokuma, J.T. Murai, M.D. West.
2. Australia Patent 729377 (granted May 17, 2001). Methods and Materials for the Growth of Primate-Derived Primordial Stem Cells in Feeder-Free Culture. Geron Corporation, A.G. Bodnar, **C.-P. Chiu**, J.D. Gold, M. Inokuma, J.T. Murai, M.D. West.

Publications

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2. Blau, H.M., C. Webster, **C.-P. Chiu**, S. Guttman and F. Chandler (1983) Differentiation properties of pure populations of human dystrophic muscle cells. *Exp. Cell Res.* 144:495-503.
3. Blau, H.M., **C.-P. Chiu** and C. Webster (1983) Cytoplasmic activation of human nuclear genes in stable heterocaryons. *Cell* 32:1171-1180.
4. Blau, H.M., **C.-P. Chiu**, G.K. Pavlath and C. Webster (1983) Muscle gene expression in hetercaryons. *Adv. Exp. Med. Biol.* 182:231
5. Blau, H.M., C. Webster, G.K. Pavlath and **C.-P. Chiu** (1983) Evidence for defective myoblasts in Duchenne Muscular Dystrophy. *Adv. Exp. Med. Biol.* 182:85-112.
6. Blau, H.M., C. Webster and **C.-P. Chiu** (1984) Cytoplasmic activation of muscle genes in stable mouse-human heterokaryons. An approach to the study of cell commitment to myogenesis. *Exp. Biol. Med.* 9:34-40.
7. Kedes, L., H.M. Blau, P. Gunning, P. Ponte, **C.-P. Chiu**, W. Bains, J. Engel and S. Guttman (1984) Molecular genetics of human myogenesis. *Exp. Biol. Med.* 9:202-210.
8. **Chiu, C.-P.** and H.M. Blau (1984) Reprogramming cell differentiation in the absence of DNA sysnthesis. *Cell* 37:879-887.
9. **Chiu, C.-P.** and H.M. Blau (1985) 5-Azacytidine-induced responsiveness to trans-acting muscle gene regulators. *Cell* 40:417-424.
10. Blau, H.M., G.K. Pavlath, E.C. Hardeman, **C.-P. Chiu**, L. Silberstein, S.G. Webster, S.C. Miller and C. Webster (1985) Plasticity of the differentiated state. *Science* 230:758-766.
11. Hardeman, E.C., **C.-P. Chiu**, A. Minty and H. Blau (1986) The pattern of actin expression in human fibroblast x mouse muscle heterkaryons

suggests that human muscle regulatory factors are produced. *Cell* 47:123-130.

12. **Chiu, C.-P.**, C. Moulds, R.L. Coffman, D. Rennick and F. Lee (1988) Multiple biological activities are expressed by a mouse interleukin 6 cDNA clone isolated from bone marrow stromal cells. *Proc. Natl. Acad. Sci. USA* 85:7099-7103.

13. Lee, F., T. Yokota, **C.-P. Chiu**, J. De Vries, J. Banchereau, N. Arai, R. Coffman, D. Rennick and K. Arai (1988) The molecular cloning of interleukins 4,5 and 6: multifunctional hemopoietic growth factors. *Behring. Inst. Mitt.* 83:8-14

14. Pavlath, G.K., **C.-P. Chiu** and H.M. Blau (1989) *In vivo* aging of human fibroblasts does not alter nuclear plasticity in heterokaryons. *Somat. Cell Mol. Genet.* 15:191-202.

15. **Chiu, C.-P.** and F. Lee (1989) IL-6 is a differentiation factor for M1 and WEHI-3B myeloid leukemic cells. *J. Immunol.* 142:1909-1915.

16. Lee,F., **C.-P. Chiu**, J. Wideman, P. Hodgkin, S. Hudak, L. Troutt, T. Ng, C. Moulds, R. Coffman, A. Zlotnik and D. Rennick (1989) Interleukin-6. A multifunctional regulator of growth and differentiation. *Ann N.Y. Acad. Sci.* 557:215-228.

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18. Billips, L.G., D. Petitte, K. Dorshkind, R. Narayanan, **C.-P. Chiu**, and K.S. Landreth (1992) Differential roles of stromal cells, interleukin-7, and *kit*-ligand in the regulation of B lymphopoiesis. *Blood* 79:1185-1192.

19. Feng, J., W.D. Funk, S.-S. Wang, S.L. Weinrich, **C.-P. Chiu**, R.R. Adams, E. Chang, R.C. Allsopp, J. Yu, M.D. West, C.B. Harley, W.H. Andrews, and B. Villeponeau (1995) The RNA component of human telomerase. *Science* 269:1236-1241.

20. **Chiu, C.-P.**, W. Dragowski, N.W. Kim, H. Vaziri, J. Yui, T.E. Thomas, C.B. Harley, and P.M. Lansdorp (1996) "Differential expression of telomerase activity in hematopoietic progenitors from adult human bone marrow." *Stem Cells* 14:239-248.

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25. Bodnar, A.G., M. Ouellette, M. Frolkis, Sh.E. Holt, **C.-P. Chiu**, G.B. Morin, C.B. Harley, J.W. Shay, S.Lichtsteiner, and W.E. Wright. (1998) "Extension of life-span by introduction of telomerase into normal human cells." *Science* 279:349-352.

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28. Yang, J., Chang, E., Cherry, A.M., Bangs, C.D., Oei, Y., Bodnar, An., Bronstein, A., **Chiu, C.-P.**, and G.S. Herron (1999) "Human endothelial cell life-extension by telomerase expression." *J. Biol. Chem.,* 274:26141-26148.

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WO09920741A1 04/29/1999 METHODS AND MATERIALS FOR THE GROWTH OF PRIMATE-DERIVED PRIMORDIAL STEM CELLS